

***Remarks***

Reconsideration of this Application is respectfully requested.

Upon entry of the foregoing amendment, claims 21-42 are pending in the application, with claim 21 being the independent claim. Claim 21 is amended, in accordance with the Examiner's suggestions. Support for this amendment can be found, *inter alia*, at page 23, line 15 to page 24, line 2. This amendment is believed to place the claims in condition for allowance. These changes are believed to introduce no new matter, and their entry is respectfully requested.

Based on the above amendment and the following remarks, Applicant respectfully requests that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

***Rejections under 35 U.S.C. §§ 101 and 112***

Claims 21-42 were rejected under 35 U.S.C. §§ 101 and 112 for alleged lack of utility. Applicants have amended claim 21, from which claims 22-42 depend. Applicants respectfully traverse this rejection.

The Office Action stated that

there is no nexus between the TIF-2 and any diseases or diagnostic uses and thus the protein lacks a well established utility. The specification on page 6 discloses the use of the TIF-2 to understand the mechanism underlying the model for nuclear receptor modulations. However, the study of models lacks substantial utility because further research to identify or reasonably confirm a "real world" context of use is required to create a nexus to a disease. The polypeptide lacks substantial utility because further research to identify or reasonably confirm a "real world" context of use is required.

The presently claimed polypeptides have utility beyond investigation into the mechanism of nuclear receptor modulations. The inventors have shown that the polypeptide of the invention, TIF-2, binds in an agonist-dependent manner to several nuclear receptors. Nuclear receptors are a family of ligand-inducible transcriptional regulatory factors which include steroid hormone, thyroid hormone, vitamin D3 and retinoid receptors. TIF-2 interacts with several of these nuclear receptors, including RAR, RXR, ER, TR, VDR, GR and AR. *See* specification, page 37, lines 12-16. Thus, the presently claimed polypeptides have utility, *inter alia*, in transcriptional regulation.

Applicants have also described screening methods using the polypeptides of the invention to identify antagonists or agonists of nuclear receptors. *See*, for example, specification, page 34, line 8 to page 43, line 6. Although not necessary, Applicants have disclosed candidate antagonists and agonists of nuclear receptors. Specification, page 38, lines 12-30. The specification points out the importance of methods of screening for agonists and antagonists of nuclear receptors. For example, antagonists and agonists of certain nuclear receptors have been shown to have inhibitory effects on cancer cells. Specification, page 36, line 22 to page 37, line 11. Applicants assert that using the polypeptides of the invention to screen for possible cancer therapeutics is a "real world" use of such polypeptides.

An assay for identifying potential therapeutic compounds defines a "real world" context of use. *See* M.P.E.P. § 2107.01 (I.) at 2100-32 (Eighth edition, First Revision, February 2003). In the present case, Applicants have identified a compound useful in an assay to identify, *inter alia*, therapeutic compounds for cancer. Thus, the presently claimed polypeptides have a specific, substantial use.

Applicants believe the present claims meet the requirements of 35 U.S.C. § 101. Accordingly, withdrawal of this rejection is respectfully requested.

The Office Action states that claims 21-42 are rejected under 35 U.S.C. § 112, first paragraph "since the claimed invention is not supported by either a substantial asserted utility or a well established utility . . . one skilled in the art clearly would not know how to use the claimed invention." Paper No. 9, page 4. Applicants assert that the claimed invention is supported by a specific and substantial utility, and complies with the requirements of 35 U.S.C. § 101 as described above. The Examiner "should not impose a 35 U.S.C. § 112, first paragraph, rejection grounded on a 'lack of utility' basis unless a 35 U.S.C. 101 rejection is proper." M.P.E.P. § 2107.01 (IV.) at 2100-36 (Eighth edition, First Revision, February 2003). Because the claimed invention complies with the utility requirement of 35 U.S.C. § 101, the rejection under 35 U.S.C. § 112, first paragraph, based on the alleged lack of utility of the claimed invention, should be not be maintained. Applicants therefore respectfully request that this rejection be withdrawn.

***Rejections under 35 U.S.C. § 112***

Claims 21 and 36-42 were rejected under 35 U.S.C. § 112, first paragraph, for alleged lack of written description. Applicants respectfully traverse this rejection as it may be applied to the pending claims.

The Office Action stated that

the essential feature of the invention is the specific TIF-2 with specific amino acid sequence. "TIF2 protein activity" encompasses generic such general function as ionic changes of the protein due to pH change in the buffer. *University of California v. Eli Lilly and Co. (CAFC) 43 USPQ2d 1398* held that a generic claim to human or mammalian when only the rat protein sequence was disclosed did not have written description in the

specification. Thus, the specification does not have written description for the genus of TIF-2 with general functional limitation.

Paper No. 9, page 4.

Contrary to the assertion in the Office Action, ionic changes of the protein due to pH change in the buffer is not an activity of a protein, but a *characteristic* of a protein. An activity of a protein is action the protein performs, such as binding to another protein or activation of a biological function, not a property of the protein, such as ionic change or melting point.

Additionally, the present case is distinguishable from *University of California v. Eli Lilly and Co.*, 43 U.S.P.Q.2d 1398 (Fed. Cir. 1997), *cert. denied*, 523 U.S. 1089 (1998). In *University of California v. Eli Lilly*, the issue was whether the disclosure of a rat cDNA insulin sequence was sufficient to support a claim directed to a generic mammalian insulin sequence. According to the court,

[a] description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus.

*University of California v. Eli Lilly and Co.*, 43 U.S.P.Q.2d 1398 (Fed. Cir. 1997).

In the present case, the claims are not directed to an unspecified sequence identified solely by function. In the present case, structural features common to members of the genus are indeed defined in the claims, i.e., the specific sequence recited in the claims. All member of the genus have a sequence which is at least 90% identical to the specific sequence.

The Office Action stated that "[i]t is suggested that the functional limitation include function of interaction with nuclear receptors with support in the specification which does not introduce new matter." Paper No. 9, page 4. Applicants have amended claim 21, from which claims 36-42 depend, to specify that the polypeptide have at least one activity selected from the group consisting of binding to a nuclear receptor and enhancing transcription. Support for this amendment can be found at least at page 23, line 15 to page 24, line 2.

Applicants believe the present claims are in condition for allowance. Accordingly, withdrawal of this rejection is respectfully requested.

### ***Conclusion***

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicant therefore respectfully requests that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicant believes that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

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Appl. No. 09/842,256

Prompt and favorable consideration of this Amendment and Reply is respectfully  
requested.

Respectfully submitted,

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